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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No. 09/977,155
Applicant: Herz et al.
Filed: October 12, 2001
Docket No. UTSD:0862
Title: *LDL Receptor Signaling Assays*

Customer No. 23379
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Group Art Unit: 1641
Examiner: Cook, L.

CERTIFICATE OF TRANSMISSION
I hereby certify that this corr is being transmitted by facsimile to the Comm for Patents 703-872-9306 on June 25, 2005.

Signature _____
Richard Aron Osman

AFTER-FINAL RESPONSE

Commissioner for Patents
Washington, DC 20231

Dear Examiner Cook:

Thank you for the Advisory Action dated Jun 16, 2005.

35USC102(b)

Willnow et al. (1994, J Biol Chem 269, 15827-32) describe the production and functional analysis of truncated LRPs comprising subsets of the of the native N-terminal, extracellular domains (Fig. 1). One minireceptor was partially cleaved at a known region IV proteolytic processing site (Fig. 2A, lanes 2 and 4). LRP is known to be naturally proteolyzed at this extracellular N-terminal proteolytic processing site to generate two subunits: a 85 kd membrane spanning beta subunit, and a larger 515 kd N-terminal alpha-subunit which lacks a membrane-spanning region, but remains attached to the membrane through noncovalent association with the smaller C-terminal beta-subunit (Herz et al. (1990, EMBO J 9, 1769-1776).

The present inventors disclose that LRP and other members of the LDL receptor gene family undergo distinct endoproteolytic processing events *that result in the release of their cytoplasmic tails into the cytoplasm.* Specification, p.1, liens 24-26. To release a cytoplasmic tail, the disclosed processing need to occur at intramembranous or cytoplasmic sites – not the N-terminal, extracellular region IV processing site known in the art, which liberates an extracellular domain, and not a cytoplasmic tail.

Accordingly, all our claimed methods are for detecting proteolysis of an LDL receptor